

Amendments to the Specification

Please replace the existing Sequence Listing (pages 1-37), filed September 15, 2000, with the substitute Sequence Listing (pages 1-37) submitted herewith and insert the same at the end of the application.

Please replace the paragraph beginning at page 119, line 27 with the following paragraph:

Cytokine induced tyrosine phosphorylation of other Jaks activates their in vitro kinase activity (Witthuhn *et al.*, *Cell*:227-236 (1993); Artgetsinger *et al.*, *Cell* 74:237-244 (1993); Silvennoinen, *Proc. Natl. Acad. Sci. USA* 90:8429-8433 (1993); Muller *et al.*, *Nature* 366, 129-135 (1993); Stahl *et al.*, *Science* 263:92-95 (1994)). We therefore examined the effects of IL-2 or IL-4 Jak1 or Jak3 kinase activity. The tyrosine phosphorylation of Jak1 was not associated with the activation of demonstrable kinase activity in immunoprecipitates comparable to the response seen to EPO (Witthuhn *et al.*, *Cell*:227-236 (1993)). However, tyrosine phosphorylation of Jak1 in the response to IL-6 or CNTF is associated with activation of kinase activity (Stahl *et al.*, *Science* 263:92-95 (1994); Narazaki *et al.*, *Proc. Natl. Acad. Sci. USA*, in press, (1994)). Jak3 kinase activity was not detected in immunoprecipitates with the Jak3 specific anti-peptide antiserum. However, this antiserum is against a peptide containing the putative autophosphorylation site (KDYY) (SEQ ID NO:17) which may interfere with kinase activity as well as immunoprecipitation. We therefore assayed immunoprecipitates

obtained with the Jak1/Jak3 cross-reactive antiserum against Tyk2. Activation of in vitro kinase activity was readily detectable in immunoprecipitates from cells stimulated with either IL-2 or IL-4 (Fig. 9B). Moreover, there was a single phosphorylated protein in the Jaks size range which co-migrated with Jak3. No detectable phosphorylation of a protein migrating at the position of Jak1 was seen, consistent with the results obtained with the Jak1 specific antiserum. Amino acid analysis of the in vitro phosphorylated protein indicated that phosphorylation occurred exclusively on tyrosine.